

Exhibit 33

From: "OMahony, Kevin" <kevin.omahony@novartis.com>
To: xavier <xavier@huahaipharma.com>, tangyinhu <tangyinhu@huahaipharma.com>, "Quinn, Jannine" <jannine.quinn@novartis.com>, chenyingzhi@huahaipharma.com, "Breen, Sarah" <sarah.breen@novartis.com>, "Hu, Brad" <brad.hu@novartis.com>, "Zhu, Bin-1" <bin-1.zhu@novartis.com>, 徐覓 <xumi@huahaipharma.com>, 朱玲 <zhu ling@huahaipharma.com>, cai <cai@huahaipharma.com>, peng dong <dongpeng@huahaipharma.com>, xiongying <xiongying@huahaipharma.com>
Cc: minli <minli@huahaipharma.com>, jenson <jenson@huahaipharma.com>
Date: Thu, 07 Jun 2018 15:08:33 +0000
Attachments: Nitrosodimethylamine_es035025n.pdf (126.56 kB)

Dear All,

Please see below an update on activities at Novartis and some potential roots of synthesis provided by our R&D group.

Actions for confirmation of identity:

- Reference material for Nitrosodimethylamine has been received.
- Retention time analysis of the peak from the reference compared to the unknown in the GC and MRM using a triple quadrupole GC-MS will be performed to double check the identity. This is scheduled to be completed on Monday 11th June.
- If peak confirmed as Nitrosodimethylamine tentative quantitation of levels in three batches from which we can propose levels present in all batches tested so far.

Potential roots of formation:

1. Leaching from rubber in the process equipment
2. Upon contact with tap water that has been pre-treated by chloramination (Cl₂ and NH₃), DMF might react to NDMA. See Table 1 in the attached paper. This pathway is reasonable only if at least some oxidant (such as hypochlorite in process water) would end up in process media that contain DMF and valsartan.

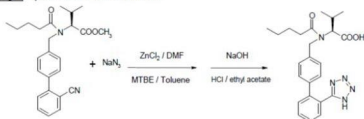
Please also make sure that any detected NDMA traces really originate from the test sample and not from water that is used in the analytical procedure. This may prove tricky in the ppb range.

3. Two chemical steps in the ROS of Huahai (Step 3 and 4) use N,N-dimethylformamide (DMF) as a solvent. DMF is known to be subject to hydrolysis, releasing dimethylamine and formic acid, in particular at elevated temperature or in presence of acids or bases.

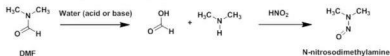
PageID: 98714

The critical step of Step 4 is the cyclization of the amide compound with sodium azide (NaN_3) to the triazole. The reaction is slow and needs high temperature over several hours. Huahai uses ZnCl_2 in DMF to avoid the use of the traditional, but ecotoxic organotin reagent (tributyltin chloride).

Step 4 Synthesis of crude Valsartan



The reaction of Step 4 requires an excess of NaN_3 which has to be destroyed in the work-up. The common method to destroy excess azide is reaction with sodium nitrite and an acid to obtain HNO_2 which transforms azide into N_2 and N_2O . If dimethylamine is present, it would react with HNO_2 to form the N-nitroso compound:



A missing piece of evidence is the method by which Huahai actually destroys the excess azide of Step 4. Is this done by addition of sodium nitrite, and is this performed in presence of the valsartan product?

Best regards,

Kevin O'Mahony

AS&T Expert,
Launch & Transfer,
External Supply Operations (ESO)
Novartis International
Pharmaceutical Ltd., Branch Ireland
IE- Ringaskiddy, County Cork
IRELAND

Phone +353 21 4862037
kevin.omahony@novartis.com
www.novartis.com

From: O'Mahony, Kevin
Sent: 07 June 2018 07:58
To: xavier; tangyinhuai; Quinn, Jannine; chenyingzhi@huahaiapharm.com; Breen, Sarah; Hu, Brad; Zhu, Bin-1; 徐亮; 朱玲; cai; peng dong; xlongying
Cc: minli; jenson
Subject: RE: Valsartan

Dear Xavier,

I fully understand. But I still think it would be a good idea to have a quick call to discuss what we see so that you can have the most up to date information.

So maybe we can dial in for 15 minutes?

Best regards,

Kevin O'Mahony
AS&T Expert
External Supply Operations (ESO)
Novartis International
Pharmaceutical Ltd., Branch Ireland
IE- Ringaskiddy, County Cork
IRELAND

Phone +353 21 4862037
kevin.omahony@novartis.com
www.novartis.com

From: xavier [mailto:xavier@huahaiapharm.com]
Sent: 07 June 2018 09:37
To: O'Mahony, Kevin; tangyinhuai; Quinn, Jannine; chenyingzhi@huahaiapharm.com; Breen, Sarah; Hu, Brad; Zhu, Bin-1; 徐亮; 朱玲; cai; peng dong; xlongying
Cc: minli; jenson
Subject: Re: Valsartan

Dear Kevin,

Thanks a lot for your invitation.

I have checked with Dr.U's team, actually it will take us some time to do study on the potential Nitrosodimethylamine impurity.

So may we suggest to postpone the TC to next week once we have more update and comments?

Certainly, if Novartis has anything new to update and share, we will appreciate it.

Best Regards

HUAHAI PHARM

PageID: 98716

Mr. Xavier Tang 汤凤扬

Regional Representative, Sales & Marketing

Add: Xunqiao, Linhai, Zhejiang 317024, China

Tel: +86-576-85016411 Fax: +86-576-85991062

Mobile: +86-13706763070

Email: xavier@huahaipharm.comLearn us more at www.huahaipharm.com**From:** O'Mahony, Kevin.**Date:** 2018-06-06 23:59**To:** [xavier](mailto:xavier@huahaipharm.com); [tangyinhua](mailto:tangyinhua@huahaipharm.com); [Quinn_Jannine](mailto:Quinn_Jannine@huahaipharm.com); [chenyingzhi](mailto:chenyingzhi@huahaipharm.com); [Breen_Sarah](mailto:Breen_Sarah@huahaipharm.com); [Hu_Brad_Zhu_Bin-1](mailto:Hu_Brad_Zhu_Bin-1@huahaipharm.com); 徐亮; 朱元; Cai peng dong; xiongying**Subject:** Valsartan

Dear All,

Please find details for a follow up call tomorrow to discuss the potential Nitrosodimethylamine impurity.

Best regards,

Kevin O'Mahony

AS&T Expert

External Supply Operations (ESO)

Novartis International

Pharmaceutical Ltd., Branch Ireland

IE- Ringaskiddy, County Cork

IRELAND

Phone +353 21 4862037

kevin.omahony@novartis.comwww.novartis.com[Click Here to Join Your Skype for Business Meeting](#)

After your meeting, let us know how your meeting experience was with Skype for Business technology:

Was it [Good](#) or [Bad](#) ? (click one)

This survey will be available for a limited time and the information provided will help us improve our service.

PageID: 98717

Connecting via Phone?**iPhone:** Press a number for one-touch dialing**Telephone:** Dial and enter the conference ID when prompted: 273 278 928

Australia, Sydney	+61282784329
Austria	+4313602775440
Brazil	+551138788274
Canada, Toll Free	+18338175826
China, Beijing	+861057843521
France	+33185148569
Germany	+4991194893660
India Hyderabad	+914039406980
Ireland	+35315339883
Italy	+390238594059
Japan, Tokyo	+81366344751
Mexico	+525550912421
Russia	+74957820833
Singapore	+6564288479
Slovenia	+38618888587
Spain	+34930038015
Switzerland	+41615478009
United Kingdom	+442076608417
USA, Georgia	+14047195218
USA, Massachusetts	+16172777818
USA, New Jersey	+19733556538
USA, Texas	+18179533373

Additional phone numbers: View the [global phone list](#)**Connect via the Web:** [Join Now](#)**No local number?:** Use the [Call me at](#) feature ([external access](#))**Meeting organizers:** [Set/reset your PIN](#) if needed**Learn more about Skype:** at [Novartis](#), on [Yammer](#), or on the [Web](#)**Learn more about collaboration tools:** [Visit the Virtual Collaboration Toolkit](#)**Tip:** For the best meeting experience, use an [approved headset/speaker](#) and a wired Internet connection, when available.

